

Application of: Pittenger, et al
Serial No.: 09/319,521
Filed: June 4, 1999
For: Improved Chondrogenic Differentiation of Human Mesenchymal Stem Cells



Group: 1644

Examiner: Tung

1644
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Assistant Commissioner of Patents
Washington, D.C. 20231

Sir:

In response to the restriction requirement dated September 25, 2000, Applicants elect to prosecute the invention of Group II, as defined in Claims 14-35, 37, 38, 40, and 41. Applicants also elect, as a specific chondroinductive agent, a member of the TGF-Beta superfamily. This election is made with traverse.

Respectfully submitted,

Raymond J. Lillie, Esq.
Registration No. 31,778

	D 0422		D 2429	D 2554					
	[1X]	D 1152	[10X]	[10X]	D 2902	D 3656	D 5030	D 5280	D 5523
COMPONENT	g/L	g/L	g/L	g/L	g/L	g/L	g/L	g/L	g/L
INORGANIC SALTS									
CaCl ₂ •2H ₂ O	0.265	0.265	2.65	2.65	0.265	0.265	0.265	0.265	0.265
Fe(NO ₃) ₃ •9H ₂ O	0.0001	0.0001	0.001	0.001	0.0001	0.0001	0.0001	0.0001	0.0001
MgSO ₄	0.09767	0.09767	0.9767	0.9767	0.09767	0.09767	0.09767	0.09767	0.09767
KCl	0.4	0.4	4.0	4.0	0.4	0.4	0.4	0.4	0.4
NaHCO ₃	3.7	—	—	—	—	—	—	—	—
NaCl	6.4	4.4	64.0	64.0	6.4	6.4	6.4	6.4	6.4
NaH ₂ PO ₄	0.109	0.109	1.09	1.09	0.109	—	0.109	0.109	0.109
Succinic Acid	—	—	—	—	—	—	—	0.075	—
Sodium Succinate	—	—	—	—	—	—	—	0.1	—
AMINO ACIDS									
L-Arginine•HCl	0.084	0.084	0.84	0.84	0.084	0.084	0.084	0.084	0.084
L-Cystine•2HCl	—	0.0626	0.626	0.626	0.0626	0.0626	0.0626	0.0626	0.0626
L-Glutamine	—	0.584	—	—	0.584	0.584	—	—	0.584
Glycine	0.03	0.030	0.30	0.30	0.030	0.030	0.030	0.030	0.030
L-Histidine•HCl•H ₂ O	0.042	0.042	0.42	0.42	0.042	0.042	0.042	0.042	0.042
L-Isoleucine	0.105	0.105	1.05	1.05	0.105	0.105	0.105	0.105	0.105
L-Leucine	0.105	0.105	1.05	1.05	0.105	0.105	0.105	0.105	0.105
L-Lysine•HCl	0.146	0.146	1.46	1.46	0.146	0.146	0.146	0.146	0.146
L-Methionine	—	0.030	0.30	0.30	0.030	0.030	0.030	0.030	0.030
L-Phenylalanine	0.066	0.066	0.66	0.66	0.066	0.066	0.066	0.066	0.066
L-Serine	0.042	0.042	0.42	0.42	0.042	0.042	0.042	0.042	0.042
L-Threonine	0.095	0.095	0.95	0.95	0.095	0.095	0.095	0.095	0.095
L-Tryptophan	0.016	0.016	0.16	0.16	0.016	0.016	0.016	0.016	0.016
L-Tyrosine (free base)	—	—	—	—	—	—	—	0.072	—
L-Tyrosine•2Na•2H ₂ O	0.10379	0.10379	1.0379	1.0379	0.10379	0.10379	0.10379	—	0.10379
L-Valine	0.094	0.094	0.94	0.94	0.094	0.094	0.094	0.094	0.094
VITAMINS									
Choline Bitartrate	—	—	—	—	—	—	—	0.0072	—
Choline Chloride	0.004	0.004	0.04	0.04	0.004	0.004	0.004	—	0.004
Folic Acid	0.004	0.004	—	—	0.004	0.004	0.004	0.004	0.004
myo-Inositol	0.0072	0.0072	0.072	0.072	0.0072	0.0072	0.0072	0.0072	0.0072
Niacinamide	0.004	0.004	0.04	0.04	0.004	0.004	0.004	0.004	0.004
D-Pantothenic Acid•½Ca	0.004	0.004	0.04	0.04	0.004	0.004	0.004	0.004	0.004
Pyridoxal•HCl	—	0.004	—	—	0.004	0.004	0.004	0.004	0.004
Pyridoxine•HCl	0.004	—	0.04	0.04	—	—	—	—	—
Riboflavin	0.0004	0.0004	0.004	0.004	0.0004	0.0004	0.0004	0.0004	0.0004
Thiamine•HCl	0.004	0.004	0.04	0.04	0.004	0.004	0.004	0.004	0.004
OTHER									
D-Glucose	4.5	4.5	10.0	45.0	1.0	4.5	—	1.0	1.0
HEPES	—	5.958	—	—	—	—	—	—	—
Phenol Red•Na	0.0159	0.0159	0.159	0.159	—	0.0159	—	0.0093	0.0159
Pyruvic Acid•Na	0.11	—	1.1	1.1	0.11	—	—	0.11	0.11
ADD									
Glucose	—	—	—	—	—	—	1.0	—	—
L-Glutamine	0.584	—	0.584 (1X)	0.584 (1X)	—	—	0.584	0.584	—
L-Cystine•2HCl	—	—	—	—	—	—	—	—	—
L-Leucine	—	—	—	—	—	—	—	—	—
L-Lysine•HCl	—	—	—	—	—	—	—	—	—
L-Methionine	—	—	—	—	—	—	—	—	—
NaHCO ₃	—	3.7	3.7 (1X)	3.7 (1X)	3.7	3.7	3.7	3.7	3.7
NaH ₂ PO ₄	—	—	—	—	—	0.109	—	—	—
Phenol Red•Na	—	—	—	—	—	—	—	—	—
Pyruvic Acid•Na	—	—	—	—	—	—	—	—	—
Grams of powder required to prepare 1 L	N/A	17.4	N/A	N/A	10.0	13.3	8.3	9.6	10.0

	D 5546	D 5648	D 5671	D 5796	D 5921	D 6046	D 6171	D 6429	D 6546	D 7777
	[1X]	D 6655	[1X]	[1X]	[1X]	[1X]	[1X]	[1X]	[1X]	D 6780
COMPONENT	g/L	g/L	g/L	g/L	g/L	g/L	g/L	g/L	g/L	g/L
INORGANIC SALTS										
CaCl ₂ •2H ₂ O	0.265	0.265	0.265	0.265	0.265	0.265	0.265	0.265	0.265	0.265
Fe(NO ₃) ₃ •9H ₂ O	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001
MgSO ₄	0.09767	0.09767	0.09767	0.09767	0.09767	0.09767	0.09767	0.09767	0.09767	0.09767
KCl	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
NaHCO ₃	3.7	—	3.7	3.7	3.7	3.7	3.7	3.7	3.7	—
NaCl	6.4	6.4	6.4	6.4	6.4	6.4	4.4	6.4	6.4	6.4
NaH ₂ PO ₄	0.109	0.109	0.109	0.109	0.109	0.109	0.109	0.109	0.109	0.109
Succinic Acid	—	—	—	—	—	—	—	—	—	—
Sodium Succinate	—	—	—	—	—	—	—	—	—	—
AMINO ACIDS										
L-Arginine•HCl	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084	0.084
L-Cystine•2HCl	0.0626	0.0626	0.0626	0.0626	0.0626	0.0626	0.0626	0.0626	0.0626	0.0626
L-Glutamine	—	0.584	—	0.584	—	0.584	—	0.584	—	0.584
Glycine	0.030	0.030	0.030	0.030	0.030	0.030	0.030	0.030	0.03	0.030
L-Histidine•HCl•H ₂ O	0.042	0.042	0.042	0.042	0.042	0.042	0.042	0.042	0.042	0.042
L-Isoleucine	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105
L-Leucine	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105	0.105
L-Lysine•HCl	0.146	0.146	0.146	0.146	0.146	0.146	0.146	0.146	0.146	0.146
L-Methionine	0.030	0.030	0.030	0.030	0.030	0.030	0.030	0.030	0.030	0.030
L-Phenylalanine	0.066	0.066	0.066	0.066	0.066	0.066	0.066	0.066	0.066	0.066
L-Serine	0.042	0.042	0.042	0.042	0.042	0.042	0.042	0.042	0.042	0.042
L-Threonine	0.095	0.095	0.095	0.095	0.095	0.095	0.095	0.095	0.095	0.095
L-Tryptophan	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016	0.016
L-Tyrosine (free base)	—	—	—	—	—	—	—	—	—	—
L-Tyrosine•2Na•2H ₂ O	0.10379	0.10379	0.10379	0.10379	0.10379	0.10379	0.10379	0.10379	0.10379	0.10379
L-Valine	0.094	0.094	0.094	0.094	0.094	0.094	0.094	0.094	0.094	0.094
VITAMINS										
Choline Bitartrate	—	—	—	—	—	—	—	—	—	—
Choline Chloride	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004
Folic Acid	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004
myo-Inositol	0.0072	0.0072	0.0072	0.0072	0.0072	0.0072	0.0072	0.0072	0.0072	0.0072
Niacinamide	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004
D-Pantothenic Acid•½Ca	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004
Pyridoxal•HCl	—	0.004	—	—	—	—	—	—	—	0.004
Pyridoxine•HCl	0.004	—	0.004	0.004	0.004	0.004	0.004	0.004	0.004	—
Riboflavin	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004	0.0004
Thiamine•HCl	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004	0.004
OTHER										
D-Glucose	1.0	4.5	4.5	4.5	1.0	1.0	4.5	4.5	4.5	4.5
HEPES	—	—	—	—	—	—	5.958	—	—	—
Phenol Red•Na	0.0159	0.0159	0.0159	0.0159	—	0.0159	0.0159	0.0159	0.015	0.0159
Pyruvic Acid•Na	0.11	—	—	—	—	0.11	—	0.11	0.11	0.11
ADD										
Glucose	—	—	—	—	—	—	—	—	—	—
L-Glutamine	0.584	—	0.584	—	0.584	—	0.584	—	0.584	—
L-Cystine•2HCl	—	—	—	—	—	—	—	—	—	—
L-Leucine	—	—	—	—	—	—	—	—	—	—
L-Lysine•HCl	—	—	—	—	—	—	—	—	—	—
L-Methionine	—	—	—	—	—	—	—	—	—	—
NaHCO ₃	—	3.7	—	—	—	—	—	—	—	3.7
NaH ₂ PO ₄	—	—	—	—	—	—	—	—	—	—
Phenol Red•Na	—	—	—	—	—	—	—	—	—	—
Pyruvic Acid•Na	—	—	—	—	—	—	—	—	—	—
Grams of powder required to prepare 1 L	N/A	13.4	N/A	N/A	N/A	N/A	N/A	N/A	N/A	13.5